

Product Data Sheet

Product Name: JWZ-8-103 hydrochloride

Cat. No.: GC80879

Chemical Properties

Cas. No.

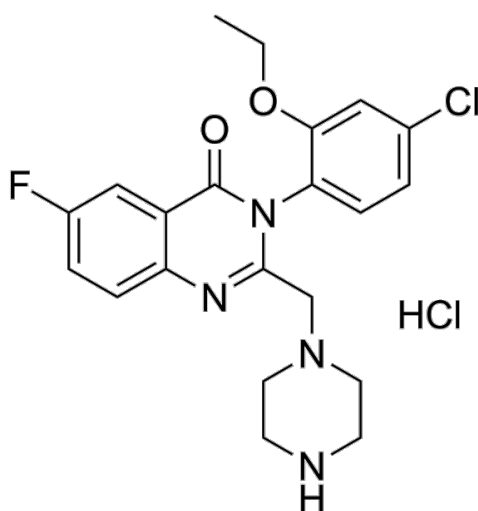
Formula $C_{21}H_{23}Cl_2FN_4O_2$ M.Wt 453.34

Solubility DMSO: 100 mg/mL (220.58 mM; ultrasonic and warming and heat to 60°C) Storage Store at 4°C, away from moisture and light

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Background

JWZ-8-103 hydrochloride is an orally active analog of PRLX-93936 and a molecular glue targeting TRIM21. JWZ-8-103 hydrochloride increases the thermal stability of TRIM21. JWZ-8-103 hydrochloride promotes rapid and efficient interaction between TRIM21 and NUP98 (the apparent EC₅₀ for ternary complex formation with the PRYSPRY domain of TRIM21 and the APD domain of NUP98 is approximately 20 μM), induces extensive ubiquitination and proteasomal degradation of numerous adjacent nucleoporins (NUPs, and thereby triggers cellular apoptosis. JWZ-8-103

Caution: Product has not been fully validated for medical applications. For research use only.

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hydrochloride can be used for the research of pancreatic cancer [1].

In Vivo, JWZ-8-103 (15-50 mg/kg; i.p.; once daily; for 21 consecutive days) hydrochloride significantly inhibits tumor growth and effectively induces targeted degradation of the nuclear pore complex in the PANC-1 pancreatic cancer xenograft model^[1]. JWZ-8-103 (15 mg/kg; i.p.; once daily; for 21 consecutive days) hydrochloride induces near-complete tumor regression in HS766T pancreatic cancer xenograft models with good tolerability^[1].

In Vitro, JWZ-8-103 (10-100 μ M; 1 h) hydrochloride enhances the thermal stability of TRIM21 protein in PANC-1 cell lysates^[1]. JWZ-8-103 (10 μ M; 1 h) functions to promote the interaction between TRIM21 and NUP98 in lysates of PANC-1 cells with TRIM21 knockout and Flag-TRIM21 re-expression^[1]. JWZ-8-103 (100 nM; 6 h) hydrochloride broadly induces TRIM21-dependent nucleoporin degradation in wild-type PANC-1 cells^[1]. JWZ-8-103 (up to 10 μ M; monitored continuously for up to 2 h) hydrochloride rapidly induces the proximity interaction between TRIM21 and NUP98 in HEK293T cells, and confirms that there is no direct interaction between TRIM21 and MCL1^[1]. JWZ-8-103 (20 μ M; for approximately 1 h) hydrochloride promotes the direct binding between TRIM21 PRYSPRY and GST-NUP98 APD in purified proteins in vitro^[1]. JWZ-8-103 (15-20 nM; 21-22 days) hydrochloride exhibits significant cytotoxicity in PANC-1 cells, and this effect depends on specific amino acid binding sites on TRIM21^[1]. JWZ-8-103 (0.5 μ M; 6 h) hydrochloride blocks mRNA nuclear export and causes the retention of MCL1 and c-MYC transcripts in the nucleus in PANC-1 cells^[1]. JWZ-8-10 (2-24 h) hydrochloride exhibits significant differential toxicity in PANC-1 and non-malignant RPE1-hTERT cells: transient treatment induces irreversible cell death in PANC-1 cells, while RPE1-hTERT cells survive and recover^[1]. JWZ-8-103 (72 h) hydrochloride exhibits potent anti-proliferative activity in wild-type PANC-1 cells (IC_{50} = 9.5 nM) and TRIM21-overexpressing H661 cells (IC_{50} < 10 nM), but loses this activity in TRIM21-knockout cells^[1]. JWZ-8-103 (for 5 days) exhibits potent activity in inhibiting cell viability and degrading NUP98, GLE1 and MCL1 proteins in TRIM21-highly expressed pancreaticobiliary organoids (HCMI PDOs, including PDM-30, PDM-31, PDM-39, PDM-166), but shows no efficacy in low-expression models^[1]. JWZ-8-103 (0.1-5 μ M; 6 h) hydrochloride exhibits activity that induces substantial degradation of nuclear pore complex proteins and short-lived anti-apoptotic proteins in PANC-1, KP3, Hs766T, and MIA

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PaCa-2 cells^[1].

References:

[1]. Yuan L, et al. Defining the Antitumor Mechanism of Action of a Clinical-stage Compound as a Selective Degradator of the Nuclear Pore Complex. Cancer discovery. 2025 Dec 02;15(12):2505-2529.

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